

### **REMARKS**

The undersigned would like to thank the examiner for time taken on April 24, 2008 to discuss via telephone the outstanding rejections in the application.

Claims 97 and 157 through 176 are pending in the application. Claims 176 has been withdrawn from consideration, and claims 97 and 157 through 175 are under examination.

Claims 97 and 166 are amended herein to recite that microchips or arrays are immobilized on the recited support. The amendment is described, for example, in original claim 59 in the application as filed, and therefore includes no new matter.

#### **The section 112, first paragraph, written description rejection**

Claims 97 and 157 through 175 were rejected under 35 USC §112, first paragraph for assertedly lacking written descriptive support in the specification. Specifically, the examiner asserted that passages in the specification on which the applicant relied for previous amendment to claims 97 and 166, wherein the term "physical barriers" was added to the claims, "teach physical separation and hydrophobic and groove barriers, the hydrophobic and groove barriers being species of physical barriers" The examiner then added, "...neither the cited passages nor the entire specification defines what is encompassed by the generic physical barrier as recited in Claims 97 and 166." [Office Action at the section 3, second to last paragraph]

In a telephone discussion with the examiner on April 24, 2008, the examiner and the undersigned discussed description of Figure 2A in the specification, specifically as it relates to physical barriers in the drawing. The examiner agreed that this description satisfies the written description requirement and the new matter rejection was withdrawn as noted in an interview summary mailed April 25, 2008.

#### **The rejection under 35 USC §102(a)**

In sections 5 through 7 of the office action, the examiner maintained rejection of claims 97, 159-160, 166, and 169-170 under 35 USC §102(a) for being directed to subject

matter assertedly anticipated by the disclosure of Datta, et al., Applied and Environmental Microbiology Jan 1993, 59:144-149 [hereinafter "Datta"]. The examiner addressed independent claims 97 and 166 alleging that Datta discloses a support comprising an array of microchips, referring to Figure 1, wherein the microchips each comprise different oligonucleotide probes immobilized on the surface and separated by a physical barrier. In this instance the examiner asserted the barrier to be space, and referred to page 145, right column, and page 146, Figure 1. The examiner further asserted that Datta discloses a support wherein microchips are arranged in rows and columns.

In response to the applicant's previous arguments, the examiner alleged that features of the claimed invention that the applicants argue are not found in the disclosure of Datta are not recited in the rejected claims. More specifically, the examiner asserted that the claims do not define any limitations on size or surface area if the microchips, support or spot of oligonucleotides. Further, the examiner asserted that the applicant's distinction between the microchip/support combination of the invention and the dot blot of Datta is based on reference to an embodiment that is not specifically claimed, and even if the claims were so limited, the examiner alleged that placing the Datta dot blots on any table or lab bench would be embraced by the claimed support.

The applicant respectfully disagrees.

Previously, the applicant has pointed out that claim 97 requires a support on which microchips are arrayed, i.e., "a support comprising an array of microchips," each microchip having an array of oligonucleotides thereon. In their arrayed positions, each microchip is separated from each other microchip by either a physical barrier or a hydrophobic surface, but still on the support and positioned in such a way so as to allow separate hybridization reactions to be carried out with each microchip and to preclude probe hybridization solutions used with one microchip to bleed over to any other microchip when used in parallel in a separate hybridization reaction with a different probe. Each of these aspects is expressly recited in the claims.

The invention of claim 97 is clearly composed of multiple components – (i) microchips on (ii) a support, wherein the microchips are arrayed on the support, and (iii) either a physical barrier or a hydrophobic surface between the individual microchips. The microchip component, a component comprising arrayed oligonucleotides bound to a first

support, is described in Example 1. At page 17, lines 11-13, the precise placement of probes in an array on a microchip is taught. Methods for carrying out this precise placement are also taught in Example I. Figures 2A and 2B, the subject matter of which is described at page 19, lines 1-14, teaches arrays of oligonucleotides on microchips and the microchips themselves arrayed on a support. This disclosure teaches that each microchip can be the same or different (page 19, lines 3 through 5). Example III teaches how the microchips can be arrayed on the support for the totality of the microchips. The drawings demonstrate separation of the microchips, with Fig 2 teaching physical barriers or hydrophobic surfaces. The same hydrophobic separation techniques are taught in Example III throughout. It is this multi-component system, as explicitly recited in claim 97, in its entirety that is the subject matter of the invention. These references to the specification are made simply to underscore what the claims expressly recite; the claims as pending do not require limitations from the specification to be imported in order to distinguish the disclosure of Datta because each component of the invention, and the invention in its entirety, is expressly recited in the claims.

The same analysis hold for the subject matter of claim 166 which also requires a support (as in claim 97) comprising multiple arrays of immobilized oligonucleotides (as in claim 97) wherein each array is separated by a physical barrier or a hydrophobic surface from every other array (also as in claim 97) and each array having oligonucleotides with different sequences attached thereto. Since it is shown above that Datta does not disclose a support of any kind having a multiplicity of arrays associated therewith and separated by the means recited in the claims, Datta cannot disclose the subject matter of claim 166.

The examiner in section 7 of the instant office action admitted that it is the applicant's position that the claims require oligonucleotides on a microchip that is then arrayed onto a support. In response, the examiner asserted that the claims are not so limited. The examiner also asserted in the same section of the office action, "even if the claims required two distinct, separable elements (which the claim does not) any table or lab bench upon which the membrane/filter is placed would be encompassed by the broadly claimed support." While the applicant disagrees that with the assertion that the claims do not require distinct elements – as discussed above, it is submitted that the claims expressly recite distinct components all of which are not found in the cited art – claims 97 and 166 are amended herein to make it more expressly apparent this invention includes two such components.

Because Datta does not disclose each and every reference limitation recited in independent claims 97 and 166, the reference cannot anticipate the recited subject matter and the rejection of these claims must be withdrawn. Moreover, since a dependent claim incorporates each limitation of a claim from which it depends (35 U.S.C. §112, fourth paragraph) the limitations of claims 97 and 166 attach to each of the dependent claims which, as explained above, Datta does not disclose. Accordingly, the rejection of all claims over the disclosure of Datta must be withdrawn.

The rejection under 35 USC §102(e)

The examiner also maintained the prior rejection of claims 97, 157-160, 163-170 and 173-175 under 35 USC §102(e) for being directed to subject matter assertedly anticipated by the disclosure of Winkler, US Patent No. 5677195 [hereinafter "Winkler"]. Specifically addressing claim 97, the examiner asserted that Winkler discloses a support comprising an array of microchips each having an array of oligonucleotide probes immobilized thereon. More specifically, the examiner made reference to a support which assertedly "comprises an array of regions (#1004 [Fig 12]) wherein each region comprises an array (i.e., plurality) of probes immobilized thereof (Column 7, lines 10-41; Column 16, lines 22-53, and Fig 12)." Further, the examiner asserted that the microchips are separated by physical barriers (referring to Column 22, lines 8-14), the regions have a predominant species of probes (referring to Column 7, lines 31-38, and thus "in other words, the region has an array of probes immobilized thereon as recited in the instant claims."

In response to arguments previously made by the applicant, the examiner asserted, as above in the rejection of claims over the disclosure of Datta, "the applicant appears to assert that the claims require two distinctly, individually constructed elements, i.e., the oligos are arrayed on a surface (microchip) and multiples of the arrayed microchips are then placed onto a second surface (support)." The examiner then alleged, as above, "the claims are not so limited" and that "the claims merely require a support comprising an array of microchips, each of which has an array of oligo."

The applicant respectfully disagrees.

As above, the applicant maintains that the claims clearly recite two components – a support comprising microchips (in the case of claim 97) or arrays (in the case of claim 166) wherein the microchips or arrays have oligonucleotides attached thereto – with the arrays being separated by specifically recited physical barriers of hydrophobic surfaces. The applicant submit that the claim makes it unambiguously clear that the microchips or arrays are on a support, the support and microchips or arrays along with the means for separation thereby making up the complete invention. Despite the applicant's position that the claims as rejected are in fact clear, both claims are amended herein to more expressly state that the microchips or arrays are immobilized on the support, thereby obviating the rejection over the disclosure of Winkler for reasons previously made of record and as discussed above in the rejection based on the disclosure of Datta.

Because Winkler cannot anticipate the subject matter of either claim 97 or 166, it cannot anticipate the subject matter of any claims depending from the independent claims and the rejection over the disclosure of Winkler must be withdrawn.

#### The rejections under 35 USC §103

The examiner also maintained rejection claims 162 and 172 under 35 USC §103 for being directed to subject matter allegedly rendered obvious by the disclosure of Winkler in view of the disclosure of Augenlicht, US Patent No. 4981783 [hereinafter "Augenlicht"]. In addition, the examiner ejected claims 161 and 171 over the disclosure of Winkler in view of the 1988 Stratagene catalog at page 39.

For reasons discussed above, the disclosure of the primary reference Winkler cannot anticipate the subject matter of the broad claims because it fails to disclose each and every limitation of these claims. Because the limitations of the broad claims attach to the subject matter of the dependent claims, Winkler cannot disclose all limitations of these dependent claims either. Adding in the disclosure of either Augenlicht or the Stratagene catalog fails to correct this deficiency in the Winkler disclosure because neither additional reference discloses arrays of oligonucleotides on physically separate microchips or arrays which are themselves immobilized (as amended herein) on a support as recited in claim 97, or multiple oligonucleotide arrays which are arrayed on a support and wherein each array is

separated from all others by a physical barrier or a hydrophobic surface as recited in claim 166.

Because the combined disclosures fail to teach each and every limitation of the invention, the combination cannot render obvious the claimed subject matter and the rejections over the disclosures of Winkler and Augenlicht or Stratagene must be withdrawn.

The section 102(b) rejection over Southern

The examiner also maintained rejection of claims 97, 158-160, 163-166, 168-170 and 173-175 under 35 USC §102(b) for being directed to subject matter assertedly anticipated by the disclosure of Southern, Genomics (1992) 13:1008-1017 (hereinafter "Southern") in view of Peterkin et al., Food Microbiology (1989) 6:281-284 (hereinafter Peterkin") for reasons previously made of record.

As previously argued, the disclosure of Southern in Fig. 3 is an arrangement of four arrays of oligonucleotides, wherein each array is identical in terms of the oligonucleotides which are attached to each array in a way that gives rise to replicate measurements of the same hybridization reaction. In this arrangement, parallel use of individual arrays in the same hybridization reaction is made possible, but parallel use in different hybridization reactions (for example using different labeled probe for hybridization reactions in individual unit arrays on the same single support) cannot be accomplished because the individual arrays described by Southern lack physical or hydrophobic barriers between unit arrays to provide separation, thereby allowing different hybridization reactions to bleed over onto other arrays. Without barriers or hydrophobic surfaces as recited in the instant claims, the complete Southern arrangement is reduced to a "single reaction" array, while the products of the instant claims, as discussed in detail above, are "multiple reaction" arrays.

The examiner admits that Southern does not teach that the individual arrays in the Southern arrangement are separated by physical or hydrophobic barriers, but then alleges that hydrophobic barriers were well known and routinely practiced in the art at the time the instant invention was made, as purportedly evidenced by the disclosure Peterkin. Thus, the examiner concluded that it would have been obvious to one of ordinary skill in the art to

apply a gridded support disclosed by Peterkin to the four-quadrant support disclosed in Southern, and that the worker of ordinary skill would have been motivated to do so for the labor-saving benefits as purportedly taught by Peterkin.

The applicant disagrees.

First, the applicant submits that, if the examiner's position were correct and use of hydrophobic barriers were well known and routinely practiced in the art, certainly Southern would have employed such a separation technique. Indeed, the Peterkin disclosure was dated 1989 and the Southern disclosure is dated about three years later in 1992. This time differential begs the question as to how Southern, certainly a person of at least ordinary skill in the art, would not have found a routinely practiced, approximately three year old technique to be useful, and therefore obvious, in order to save on labor as assertedly taught by Peterkin. If Southern, arguably someone of much more than ordinary skill in the art, did not recognize such a benefit despite having knowledge of this labor-saving technique for approximately three years, the examiner must demonstrate with proof why someone of ordinary skill in the art would have made this connection.

Second, the fact that Southern failed to recognize the purported time-saving benefit the routinely practiced method of Peterkin would provide is evidence that the examiner is combining the disclosure of Southern with non-analogous art in the Peterkin disclosure. MPEP 2141.01(a)(I) states,

"Under the correct analysis, any need or problem known in the field of endeavor at the time of the invention and addressed by the patent [or application at issue] can provide a reason for combining the elements in the manner claimed." KSR International Co. v. Teleflex Inc., 550 U.S. \_\_\_, \_\_\_, 82 USPQ2d 1385, 1397 (2007). Thus a reference in a field different from that of applicant's endeavor may be reasonably pertinent if it is one which, because of the matter with which it deals, logically would have commended itself to an inventor's attention in considering his or her invention as a whole.

The fact that the disclosure of Peterkin was known for approximately three years before Southern published is evidence that there was no need or problem known in the field of polynucleotide sequencing endeavors when the Southern work was made available. Moreover, this fact is further evidence that at least Southern did not believe this well known

and routinely practiced technique logically commended itself to Southern's attention, again, a person presumably at least of ordinary skill in the art.

The applicant therefore submits that there is no evidence supporting an assertion that the instant invention would have been obvious at the time the invention was made. Indeed, the facts support a position that the worker of ordinary skill in the art would have not been motivated to combine the disclosure of Peterkin with the work of Southern because Southern did not see fit to do so. Accordingly, the applicant submits that the rejection of claims over the combined disclosures of Peterkin and Southern must be withdrawn.

### **CONCLUSION**

In view of the amendments and remarks made herein, the applicant submits that all claims are in condition for allowance and requests notification of the same.

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Respectfully submitted,

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